

AMENDMENTS

Claims 1 and 3-4 are pending.

Claim 2 has been cancelled.

Claim 4 has been added.

Support for the amendments is found in the claims and specification (page 3, last paragraph through page 4, line 30), as originally filed. No new matter is believed to have been added.

REMARKS AND REQUEST FOR RECONSIDERATION.

Applicants wish to thank the Examiner and his Supervisor for the meeting on April 1, 2008. The subject of the meeting included the prior art rejection. Applicants' representative explained that the claimed and prior art compounds have a different structure and it cannot be foreseen from known perfumes that specific modifications would have led to a compound having superior musky sent and improved stability. The Examiners indicated that the rejection would be likely withdrawn. The Examiners indicated that the final determination would require an additional prior art search.

In response to the rejection of claim 2 under 35 U.S.C. 112, second paragraph, applicants cancel claim 2 and request that the rejection be withdrawn.

Claims 1-3 are rejected under 35 U.S.C. 103(a) over Eh et al., US 6,573,391.

The rejection is traversed because

- (1) the claimed ether lactone has a different structure, and
- (2) it cannot be foreseen from known perfumes that specific modifications would have led to a compound having a strong musky sent or improved stability.

The Examiner is of the opinion that the claimed and Eh et al.'s compounds have close structural similarities and, therefore, one would have expected that the compounds would have had similar properties (page 3 of the Official Action).

In response, Applicants point out that the claimed ether lactone structure is different from the ether lactone described by Eh et al., which requires an oxygen group two positions away from the carbonyl group instead of carbon. In addition, the Eh et al. structure does not comprise a second oxygen group eleven positions away from the carbonyl as in the claimed lactone; the second oxygen in Eh et al. is two positions away from carbonyl. In addition, in the claimed lactone a methyl group is introduced two positions away from carboxyl and between two oxygen groups, while there is no methyl group in the same position in the Eh et al. compound.

A substitution of "O" for "C" is not a recognized equivalent substitution and, therefore, is not obvious. Further, the lactone ring is not planar and can adopt various conformations, e.g., envelope, chair (*see* the attached Sawant et al., J. Chem. Soc., Perkin Trans., 1:25-37-42 (1999), showing conformational changes of a lactone ring depending on oxygen position, substitutions, length of the ring, and optical isomerization, figs. 1-3 and page 2541, top of the right col.). Various conformational problems arise in lactone rings of different length having oxygen and other substituents in different positions (*see* the attached "Chemistry Rules, 2006, pages 14-15, accessed at <http://www.rjclarkson.demon.co.uk>). Alvarez-Larena et al. also describe various non-planar conformations of a lactone ring of a different length (fig. 4, page 1314, top of the right col.). Marzalek et al., PNAS, 96:7894-98 (1999) show that a distance between oxygen atoms and positions of the atoms in the pyranose ring dictate ring conformations. Thus, "ring walking" with oxygen atoms and adding a methyl group in various ring positions will likely interfere with H-H interactions in the ring and cause sterical hindering of hydrogens, oxygens, and other substituents across the ring and, therefore, cause the lactone ring conformation to change.

It has recently been shown that a single odorant molecule is typically recognized by multiple receptors, but each odorant molecule triggers a unique combination of receptors (*see*

fig. 8 of the attached Nobel Lecture “Unraveling the sense of smell” by Linda Buck, December 8, 2004, obtained from <http://www.hhmi.org/research/nobel/buck.html>, accessed 3/13/2008). Thus, olfactory receptors require an odorant molecule to have a correct 3D conformation.

Further, different combinations of receptors identify a multitude of odorants similar to the way different combinations of letters form words (page 275 of the Buck’s Lecture). A tiny shift in the chemical structure of an odorant molecule can dramatically alter its receptor code and, thereby, our perception of the odorant changing, for example, from sweaty to orange (page 275 of the Buck’s Lecture). For example, pairs of acids and alcohols that differed by a single functional group invariably had different receptor codes (see Fig. 8 and 9).

Even isomers of the compounds having the same chemical formula can have dramatically different olfactory properties. For example, various R and S isomers of (E)-3,3-dimethyl-5-(2,2,3-trimethylcyclopent-3-en-1-yl)-4-penten-2-ol have different smell, e.g., milky and strong sandalwood-like, sandal cedar, strong sandalwood, weak and flat sandal, pleasant and unpleasant odors with a faint animal note (see Aida et al., US 5,994,291, col. 2, lines 12-26).

Also, d-carvone and l-carvone have dramatically different odors (see Merck catalog, page 308).

Moreover, signals from different odorant receptors overlap in the cortex and each neuron in the cortex receives information from multiple receptors types, i.e., it may recombine signals from the different receptors that recognize a single odorant, potentially recreating an odor image from its parts (page 275-280 of the Buck’ Lecture). Thus, the mechanism of odor recognition is very complex.

The present specification describes that it would not have been foreseeable that the claimed compounds would have had intense musky sent and excellent stability in cosmetic formulations (pages 2-3) because olfactory characteristics of known fragrances do not automatically permit conclusions regarding properties of structurally related compounds, since neither the mechanism of sent perception nor the effect of the chemical structure on sent perception have been adequately researched. It cannot be predicted as to whether a modified structure of known perfumes actually causes the olfactory characteristics to be modified or as to whether these modifications are assessed positively or negatively by one skilled in the art (page 3). For example, compounds described by Wricht in "Perf. And Essential Oil Record" (58(9):648-50 (1967), fig. 1, (previously submitted) exhibit merely "an average musky sent." It would not have been foreseeable that the claimed ether lactones would have had a strong musky sent and good stability based on the compounds' structure and as a result of introduction of a methyl group at an entirely specific position (page 3 of the specification).

Therefore, one would not have reasonably expected that the specifically modified compounds would possess the intense musky sent and excellent stability based on structural and olfactory characteristics of known fragrances.

Thus, Eh et al. does not make the claimed ether lactones obvious.

Respectfully submitted,

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